REMARKS

Status of the Claims

Claims 26, 43 and 60 are currently amended.

Claim 37 is withdrawn.

Claims 1-25, 27-34, 38, 39, 42, 44-56, 62 and 64 are cancelled.

Claims 26, 35-37, 40, 41, 43, 57-61 and 63 are pending examination in this application.

Claim Amendments

Claim 26 has been amended by incorporating the limitations of claim 42 and by deleting the term "typically". The amendments to claims 43 and 60 were made to secure proper dependency from claim 26.

Claim Rejections for Indefiniteness

Claims 26, 35, 36, 40-43, 57-61, 63 and 64 were rejected as indefinite because of the claim terms "typically" and "greater". Claim 26 has been amended to delete the offending term "typically". The term "greater" in the context of claim 26 is definite. Claim 26 recites as step c: "determining, from the comparison in step (b) if the amount of β-amyloid variant determined in step (a) is *greater* than the amount of said variant present in control samples, that the patient is susceptible to or at risk of AD." Claim 26 step c clearly provides the basis of comparison which is easily understood by one of ordinary skill in this art especially in light of the specification (in particular Example 3). Claim language involving the relative term "greater" or similar relative terms are routinely used in this art (diagnosing or assessing the risk of AD) and the medical art in general in assessing the presence of some condition or element in relation to a control. *See e.g.*

claims involving assessment of AD in US 7,052,852 (*increased* ratio compared to control); 6,130,048 (an *increase* in cystatin C levels relative to normal); 6,461,831 (a relatively *greater* affinity for WGA than an AChE with an unaltered glycosylation pattern); and 6,962,793 (*increase* of hK6 compared with amount for the healthy control). Applicants request that the rejection for indefiniteness be withdrawn.

Claim Rejections for Lack of Enablement

Claims 26, 35, 36, 40-43, 57-61, and 63 were rejected as failing to comply with the enablement requirement. Specifically, the Examiner is of the view that the specification does not provide enabling support for the general collection of diseases associated with β-amyloid formation and aggregation (e.g. DLB, Cogn, MCI-AD) other than Alzheimer's disease. Claim 26 has been amended to refer only to Alzheimer's disease consistent with the examiner's acknowledged scope of enablement.

The present invention relates to a method for the early detection of certain N-terminal truncated forms of β-amyloid in patients, which aids in the determination of whether the patient may be susceptible to or at risk of Alzheimer's disease (AD). Presently, the only means for conclusive confirmation of AD is post mortem examination of the brains of AD diagnosed patients for the presence of cerebrovascular amyloid deposits and neurofibrillary tangles. Conclusive diagnosis of AD in a living patient is not possible. Diagnosis of probable AD in a live patient is essential so that early treatment can be introduced. The present invention provides an assay of CSF from live patients to aid in the determination of whether the patient may be susceptible to or at risk of developing Alzheimer's disease (AD).

Applicant has shown that the claimed N-terminal truncated and post-translationally modified $A\beta_{42}$ variants comprise a significant amount of the β-amyloid plaques from the brains of both an infraclinical AD patient (Specification, Fig. 3), and a patient with full blown AD (Specification, Fig. 2 and Table 3). Further, Applicant has demonstrated the presence of N-terminal truncated $A\beta_{42}$ peptides in the CSF of living patients with various stages of AD pathology (Specification, Table 8). Thus, Applicant's disclosure is sufficient to enable practitioner's to use the specified N-terminally truncated/post-translationally modified $A\beta_{42}$ peptides as an aid to determine whether a patient is susceptible to or at risk of developing AD.

Conclusion

The Applicant does not believe that any other fees are due. However, should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed materials, the Commissioner is authorized to deduct said fees from Deposit Account No. 08-3038/**11362.0039.NPUS01**.

Respectfully submitted,

Patricia A. Kammerer
Reg. No. 29,775
Attorney for Assignee
INNOGENETICS N.V.

Customer No. 23369
HOWREY LLP
1111 Louisiana, Suite 2500
Houston, Texas 77002
(713) 787 1400

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